Trilateral Project B3b
Mutual understanding in search and examination

Comparative study on biotechnology patent practices

Theme: Nucleic acid molecule-related inventions whose functions are inferred based on homology search

1. Introduction

Recently, the number and complexity of nucleic acid molecule-related inventions have been increasing and changing with the progress of research and development projects such as the Human Genome Project. As a result, intellectual property protection for nucleic acid molecule-related inventions whose functions are inferred based on their similarities to known DNA sequences obtained by conventional computer search (homology search) has been attracting attention.

Therefore, at the last Trilateral Technical Meeting in Tokyo, the Trilateral Offices agreed to conduct a further comparative study on nucleic acid molecule-related inventions, whose functions are inferred based on their similarities to known DNA sequences obtained by conventional computer search (homology search). The comparative study was conducted based on "TRAINING MATERIALS FOR INTERIM WRITTEN DESCRIPTION AND UTILITY GUIDELINE" from the USPTO and "Examples of examinations on the inventions related to genes" from the JPO.

2. Provision

Applicable Sections / Articles of respective Patent Laws

	Industrial applicability (Utility*)	Enablement requirement	Inventive step Non-obviousness
USPTO	***101**	**112**	**103**
EPO	**57**	**83**	**56**
JPO	**29(1)**	**36(4)**	**29(2)**

(*): In the USA, industrial applicability is not coextensive with the utility requirement of Title 35 USC. National stage applications are examined whether an invention has industrial applicability or not.

3. Question

3.1 Question (Basic question)

The answers to the following questions are intended to set forth the perspective of each

Office in addressing the Industrial applicability (Utility) and Enablement requirements of nucleic acid molecule-related inventions.
Please show the answer to each question.

No.1 : How does your Office treat an invention claiming a nucleic acid molecule, as a compound or as information?

No.2 : What kind of function or utility does your Office require to be described in the specification?

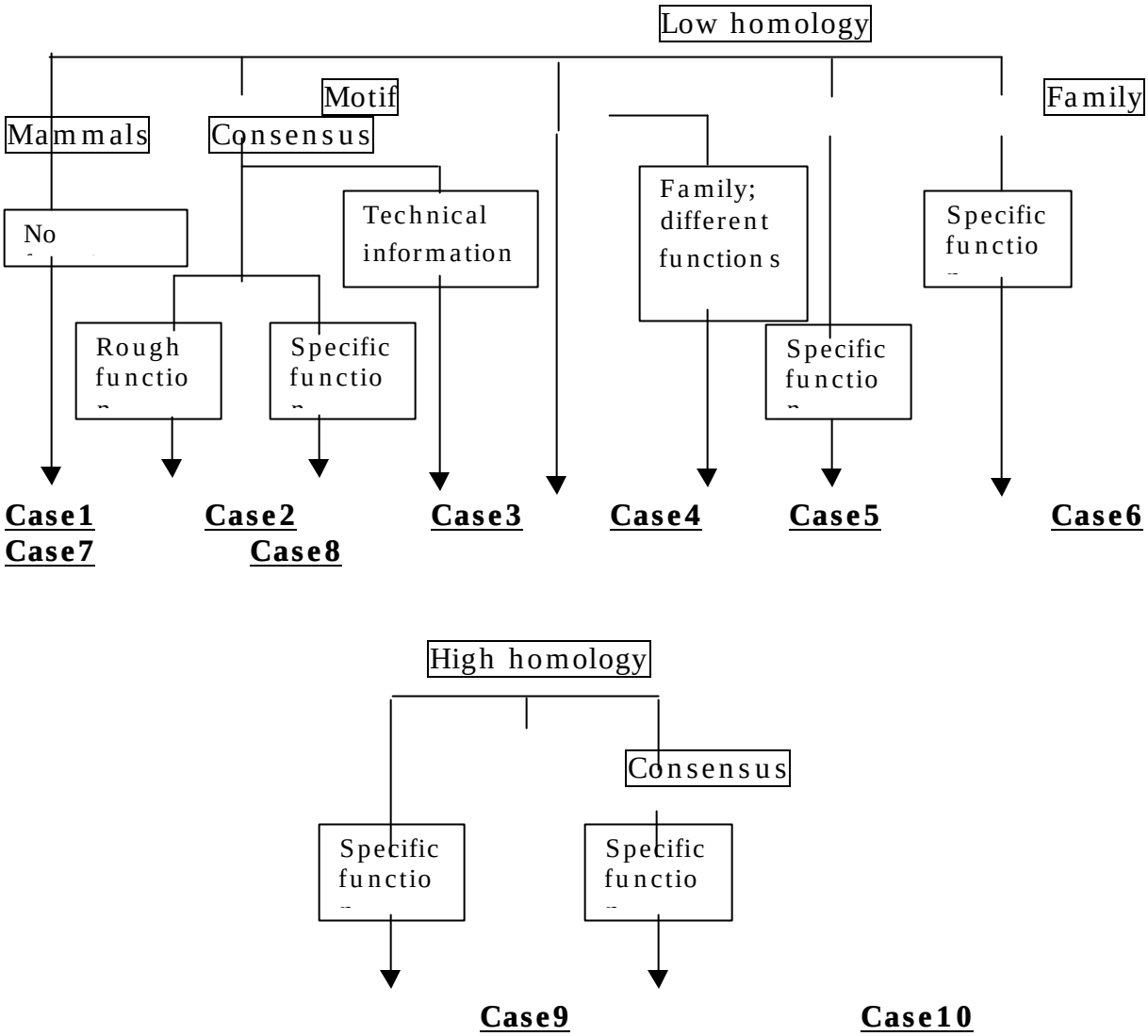
No.3 : What types of information are needed to comply with your Office's Industrial applicability (Utility) or Enablement requirement standards?

No.4 : Under what circumstances, if any, does your Office require experimental evidence demonstrating function or utility of a claimed nucleic acid molecule?

3.2 Question (Hypothetical cases) [Industrial applicability (Utility), Enablement and Inventive step (Non-obviousness)]

Please provide a detailed analysis showing how your Office would determine whether the examples below comply with your Office's Industrial applicability (Utility), Enablement, and Inventive step (Non-obviousness) requirements. If you have some supplements, please show them after each analysis.

Outline of the hypothetical cases



4. Summary of Answers

4.1 Basic question

USPTO

The USPTO treats nucleic acid molecules as chemical compounds (compositions of matter). In order to comply with the utility requirement (35 U.S.C. § 101), an invention must be supported by a specific, substantial, and credible utility. In order to comply with the enablement requirement (35 U.S.C. § 112, first paragraph), the USPTO requires a specification to disclose sufficient information such that one skilled in the art can make and use the invention based upon the disclosure present in the application coupled with information known in the art without undue experimentation. The USPTO does not have any *ab initio* requirement for experimental evidence to demonstrate the function or utility of any invention. The burden of proof in the establishing unpatentability is on the examiner. The examiner must establish a prima facie case before the burden is shifted to the applicant.

EPO

According to EPO practice, a claim to a nucleic acid molecule is a product claim to biological material (compound). The EPO requires that the function performed by a claimed sequence and the protein it encodes should be certain to the degree that a specific utility for the sequence becomes apparent beyond the realm of speculation. The claims on proteins encoded by nucleotide sequences that have not even been expressed in a host (typically a bacterial, yeast or animal cell line) are very likely not to satisfy the enablement requirement for the same reasons that cannot satisfy the requirement for industrial application. If the alleged function of a claimed nucleic acid molecule is not credible beyond mere speculation the EPO will request experimental evidence demonstrating the function in accordance with Rule 27(1)e EPC.

JPO

The JPO treats a nucleic acid molecule as a compound. The JPO requires a function from which we can assume the specific utility (the specific function) or the specific function recognized from the common general knowledge as of the filing. The applicants are required to provide information which can indicate the claimed polynucleotide probably encodes a certain functional protein. The JPO requests experimental identification when the claimed polynucleotide is not proved as encoding a certain functional protein by written argument or from the common general knowledge as of the filing.

4.2 Hypothetical cases [Industrial applicability (Utility), Enablement and Inventive step (Non-obviousness)]

The three offices showed the same views that Cases 1-2, 5-7 do not meet patentability requirements. The three offices also concurred in that there is no reason for rejection to Case 4 under some circumstances.

Case 1-2

The three Offices state the claimed invention lacks Industrial applicability (Utility) and Enablement.

The EPO mentions the claimed invention does not have Inventive step.

Case 3

The EPO and the JPO share the view that the claimed invention lacks Industrial applicability (Utility) and Enablement. The USPTO mentions the claimed invention lacks Utility and Enablement case by case.

The three Offices differ from each other with respect to Inventive step / Non-obviousness.

Case 4

The USPTO and the JPO share the view that the claimed invention meets Industrial applicability (Utility) and Enablement requirements. The EPO mentions that the claimed invention meets Industrial application and Enablement case by case.

The EPO and the JPO share the view that the claimed invention does not have Inventive step case by case. The USPTO states the claimed invention meets Non-obviousness.

Case 5-7

The three Offices state the claimed invention lacks Industrial applicability (Utility) and Enablement.

The three Offices mention differ from each other with respect to Inventive Step / Non-obviousness.

Case 8

The EPO and the JPO share the view that the claimed invention lacks Industrial applicability (Utility) and Enablement. The USPTO mentions the claimed invention lacks Utility and Enablement case by case.

The EPO and the JPO share the view that the claimed invention does not have Inventive Step case by case. The USPTO states the claimed invention meets Non-obviousness.

Case 9-10

The three Offices state the claimed invention meets Industrial applicability (Utility) and Enablement requirements.

The EPO and the JPO share the view that the claimed inventions do not have Inventive step case by case. The USPTO states the claimed inventions meet Non-obviousness.

Table of results

Case	USPTO		
	Industrial Applicability*	Inventive Step Non-obviousness	Conclusion
1	No	Yes	No
2	No	Yes	No
3	Case by case	Yes	Case by case
4	Yes	Yes	Yes
5	No	Yes	No
6	No	Yes	No
7	No	Yes	No
8	Case by case	Yes	Case by case
9	Yes	Yes	Yes
10	Yes	Yes	Yes

Case	EPO		
	Industrial Applicability*	Inventive Step Non-obviousness	Conclusion
1	No	No	No
2	No	No	No
3	No	No	No
4	Case by case	Case by case	Case by case
5	No	No	No
6	No	No	No
7	No	No	No
8	No	No	No
9	Yes	No	No
10	Yes	No	No

Case	JPO		
	Industrial Applicability*	Inventive Step Non-obviousness	Conclusion
1	No	Yes	No
2	No	Case by case	No
3	No	Case by case	No
4	Yes	Case by case	Case by case
5	No	Case by case	No
6	No	Case by case	No
7	No	Case by case	No
8	No	No	No
9	Yes	No	No
10	Yes	No	No

* "Industrial applicability" includes "Utility" and "Enablement requirement"

5. Conclusion

Following points are revealed through this comparative study.

1. The three Offices showed similar results of initial examination with respect to the Utility, Industrial Applicability or Enablement requirement of nucleic acid molecule-related inventions whose protein or other functions are inferred based on their similarities to known nucleic acid sequences obtained by conventional computer search (homology search).
   - A function or a utility based on a low homology may not be , recognized as a specific function or a specific, substantial and credible utility. [*1]
   - A function or a utility based on a high homology may be sufficient to support a specific function or a specific, substantial and credible utility. [*2]

2. The three Offices showed different results of initial examination with respect to the Inventive Step or Non-obviousness of nucleic acid molecule-related inventions whose protein or other functions are inferred based on their similarities to known nucleic acid sequences obtained by conventional computer search (homology search).
   - In case of high homology, the EPO and the JPO share the same view that the claimed invention does not have Inventive Step. On the other hand, the USPTO shows that the claimed invention has Non-obviousness.

3. The initial determinations on the patentability (Utility, Industrial Applicability, Enablement requirement, Inventive step or Non-obviousness) of nucleic acid molecule-related inventions whose protein or other functions are inferred based on their similarities to known nucleic acid sequences obtained by conventional computer search (homology search) are almost the same among the three Offices in case of low homology. However, in case of high homology, the EPO and the JPO share the same decision but the USPTO shows a different decision.

It should be noted that conclusions of this study mentioned above are based on the considerations which are to be given in first office actions, and are not final patentability determinations in each of the offices, and these conclusions are based on the information which are explicitly described for these cases. Since the subject of the comparative study is extremely controversial and highly fact dependent, patentability determinations are made in the examination of several actual applications on a case by case basis.

[USPTO] [*1]: However, it is recognized that all proteins are not alike. For some proteins low homology may be sufficient to conserve function. Therefore, no general rule exists which prevents patentability merely because protein homology is low.

[*2]: However, it is recognized that protein functions are highly dependent on their tertiary structures. The folding properties of proteins are still somewhat of a mystery with much left to be learned. Therefore, even with high homology between primary structures of proteins their functions, small differences in amino acid sequence structures may affect the proteins' folding properties for some classes of protein and thus their functions may not be conserved.

[EPO][*1 and *2]:Nucleic acids and proteins are considered as chemical compounds. It follows that established patent law concerning novelty, inventive step, industrial applicability and sufficiency of disclosure of claims relating to compounds should strictly be applied. (see Rules 23b-e EPC for the application of established patent law on biotechnological inventions). This means that the patent application should contain at the filing date all information which is necessary for examination.

Later filed evidence may be taken into consideration; however, mere in silico evidence concerning expression and function of the protein, no matter whether the level of identity with known proteins is low or high, will most likely be insufficient.

In cases where the (encoded) protein and its specific function serve as a basis for the assessment of inventive step, industrial applicability, and sufficiency of disclosure, the application as filed should provide an example showing how said protein had been expressed, and indicate the specific function of the protein.

[JPO][*1 and *2]: Due account shall be taken of, for example, following points,

(i)Even if the amino acid sequence of the protein which is encoded by the claimed nucleic acid sequence (the protein is called "corresponding protein" below) has a high homology to the amino acid sequence of the known protein which has the specific function, in cases that examiners can provide a reason which the corresponding protein has a different function from that of the said known protein, for example the differences in the tertiary structure between the said two proteins, the description of the claimed invention is deemed insufficient for enabling a person skilled in the art to carry out the claimed invention.

(ii) Even if a function of the corresponding protein is inferred based on a high homology to known nucleic acid sequences, in cases that the protein which is encoded by the known nucleic acid sequence does not have a function from which the specific utility can be assumed, the description of the claimed invention is deemed insufficient for enabling a person skilled in the art to carry out the claimed invention.

Question (Hypothetical cases) [Industrial Applicability (Utility), Enablement, and Inventive Step (Non-Obviousness)]

Please provide a detailed analysis showing how your Office would determine whether the examples below comply with your Office's Industrial applicability (Utility), Enablement, and Inventive step (Non-obviousness) requirements. If you have some supplements, please show them after each analysis.

Case 1

[Claim 1] An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:1.

[Description of the invention]
The claimed polynucleotide is a 3000bp cDNA obtained from a human liver cDNA library.
It encodes a full-length protein of 1000 amino acids of SEQ ID NO:2.
A similarity search was performed, and no sequence in the database(s) searched showed over 30% similarity to the nucleotide sequence set forth in SEQ ID NO:1 or the amino acid sequence set forth in SEQ ID NO:2.
Based on the result of the similarity search, the specification asserts that SEQ ID NO:1 encodes a novel protein (SEQ ID NO:2). The specification does not disclose the specific function of the protein, however it asserts that the protein may be used in drug screening assays. The description does not disclose what disease or condition could be treated by any potential drug(s) that were identified by these assays.

[Result of the prior art search]
The prior art search did not identify any sequence with over 30% similarity to the nucleotide sequence set forth in SEQ ID NO:1 or the amino acid sequence of SEQ ID NO:2.

Case 2

[Claim 1] An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:3.

[Description of the invention]
The claimed polynucleotide is a 3000bp cDNA obtained from a human liver cDNA library.
It encodes a full-length protein of 1000 amino acids of SEQ ID NO:4.
A similarity search was performed, and no sequence in the database(s) searched showed over 30% similarity to the nucleotide sequence set forth in SEQ ID NO:3 or the amino acid sequence set forth in SEQ ID NO:4.
However, a motif search of the amino acid sequence set forth in SEQ ID NO:4 demonstrates that SEQ ID NO:4 included a DNA-binding protein motif.
Based on the result of the search, the specification asserts that SEQ ID NO:3 encodes a novel DNA-binding protein (SEQ ID NO:4). However, no DNA target is disclosed. The specification asserts that the protein may be used in drug screening assays. The description does not disclose what disease or condition could be treated by any potential drug(s) that were identified by these assays.

[Result of the prior art search]

The prior art search did not identify any sequence with over 30% similarity to the nucleotide sequence set forth in SEQ ID NO:3 or the amino acid sequence of SEQ ID NO:4.

Case 3

[Claim 1] An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:5.

[Description of the invention]
The claimed polynucleotide is a 3000bp cDNA obtained from a human liver cDNA library.
It encodes a full-length protein of 1000 amino acids of SEQ ID NO:6.
A similarity search was performed, and no sequence in the database(s) searched showed over 30% similarity to the nucleotide sequence set forth in SEQ ID NO:5 or the amino acid sequence set forth in SEQ ID NO:6.
However, a motif search of the amino acid sequence set forth in SEQ ID NO:6 demonstrates that SEQ ID NO:6 included a factor VV1 motif.
Based on the result of the search, the specification asserts that SEQ ID NO:5 encodes a factor VV1(SEQ ID NO:6). The specification asserts that a factor VV1 may be used in drug screening assays. The description does not disclose what disease or condition could be treated by any potential drug(s) that were identified by these assays.

[Result of the prior art search]
The prior art search did not identify any sequence with over 30% similarity to the nucleotide sequence set forth in SEQ ID NO:5 or the amino acid sequence of SEQ ID NO:6.
It is a common general technological knowledge that a factor VV1 has a well-established utility.

Case 4

[Claim 1] An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:7.

[Description of the invention]
The claimed polynucleotide is a 3000bp cDNA obtained from a human liver cDNA library.
It encodes a full-length protein of 1000 amino acids of SEQ ID NO:8.
A similarity search was performed, and no sequence in the database(s) searched showed over 30% similarity to the nucleotide sequence set forth in SEQ ID NO:7 or the amino acid sequence set forth in SEQ ID NO:8.
However, a motif search of the amino acid sequence set forth in SEQ ID NO:8 demonstrates that SEQ ID NO:8 included a factor UU1 motif. The specification also provides additional technical information obtained in silico (e.g., structural information) such that one skilled in the art would recognize that SEQ ID NO:8 is a factor UU1.
Based on the above information, the specification asserts that SEQ ID NO:7 encodes a factor UU1 (SEQ ID NO:8). The specification asserts that a factor UU1 may be used in drug screening assays. The description does not disclose what disease or condition could be treated by any potential drug(s) that were identified by these assays.

[Result of the prior art search]
The prior art search did not identify any sequence with over 30% similarity to the nucleotide sequence set forth in SEQ ID NO:7 or the amino acid sequence of SEQ ID

NO:8.
It is a common general technological knowledge that a factor UU1 has a well-established utility.

Case 5

[Claim 1] An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:9.

[Description of the invention]
The claimed polynucleotide is a 2400bp cDNA obtained from a human liver cDNA library.
It encodes a full-length protein of 800 amino acids of SEQ ID NO:10.
A similarity search was performed using a known DNA and amino acid database. The claimed polynucleotide showed 40% ~50% homology to the polynucleotide encoding a family of related proteins designated A,B,...V,W as described in prior art documents 1-23. The amino acid sequence set forth in SEQ ID NO:10 showed 40% ~50% homology to the amino acid sequences of the family of related proteins designated A,B,...V,W as described in prior art documents 1-23. The protein A,B,...V,W belong to a ZZ family of proteins.
Based on the result of the similarity search, the specification asserts that the claimed polynucleotide encodes a human protein that is a member of the ZZ family, and may be used to treat patients having a disease or condition related to ZZ family members. No specific disease or condition that is related to all ZZ family members is disclosed.

[Result of the prior art search]
The prior art search did not identify any sequence with over 50% similarity to the nucleotide sequence set forth in SEQ ID NO:9 or the amino acid sequence of SEQ ID NO:10.
It is a common general technological knowledge that protein A,B,...V,W have well-established utilities. However, it is not possible to assume a well-established utility based on the result that the claimed polynucleotide encodes a human protein that is a member of the ZZ family.

Case 6

[Claim 1] An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:11.

[Description of the invention]
The claimed polynucleotide is a 2400bp cDNA obtained from a human liver cDNA library.
It encodes a full-length protein of 800 amino acids of SEQ ID NO:12.
A similarity search was performed using a known DNA and amino acid database. The claimed polynucleotide showed 55% homology to the polynucleotide encoding a factor YY1 of rat as described in prior art document A. The amino acid sequence set forth in SEQ ID NO:12 showed 55% homology to a factor YY1 of rat as described in prior art document A.
Based on the result of the similarity search, the specification asserts that the claimed polynucleotide encodes a human factor YY1, and may be used to treat patients having a disease or condition related to a factor YY1. No specific disease or condition that is related to a factor YY1 is disclosed.

[Result of the prior art search]

The claimed polynucleotide showed 45% homology to the polynucleotide encoding a factor YY2 of pig and 40% homology to the polynucleotide encoding a factor YY3 of monkey. The amino acid sequence set forth in SEQ ID NO:14 showed 45% homology to a factor YY2 of pig and 40% homology to a factor YY3 of monkey. A factor YY1, YY2 and YY3 each have a different function.

The prior art search did not identify any sequence with over 55% similarity to the nucleotide sequence set forth in SEQ ID NO:11 or the amino acid sequence of SEQ ID NO:12.

It is a common general technological knowledge that a factor YY1, YY2 and YY3 have a well-established utility.

Case 7

[Claim 1] An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:13.

[Description of the invention]

The claimed polynucleotide is a 2400bp cDNA obtained from a human liver cDNA library.

It encodes a full-length protein of 800 amino acids of SEQ ID NO:14.

A similarity search was performed using a known DNA and amino acid database. The claimed polynucleotide showed 20 to 30% homology to the polynucleotide encoding a factor WW1 of mammals such as rats as described in prior art document A, B, etc. The amino acid sequence set forth in SEQ ID NO:14 showed 20 to 30% homology to a factor WW1 of mammals such as rats as described in prior art document A, B, etc.

Based on the result of the similarity search, the specification asserts that the claimed polynucleotide encodes a human factor WW1, and may be used to treat patients having a disease or condition related to a factor WW1. No specific disease or condition that is related to a factor WW1 is disclosed.

[Result of the prior-art search]

The prior art search did not identify any sequence with over 40% similarity to the nucleotide sequence set forth in SEQ ID NO:13 or the amino acid sequence of SEQ ID NO:14.

It is a common general technological knowledge that a factor WW1 has a well-established utility.

Case 8

[Claim 1] An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:15.

[Description of the invention]

The claimed polynucleotide is a 2400bp cDNA obtained from a human liver cDNA library.

It encodes a full-length protein of 800 amino acids of SEQ ID NO:16.

A similarity search was performed, and the claimed polynucleotide was found to have 30% homology to a polynucleotide encoding a DNA ligase. An alignment of SEQ ID NO:16 with known amino acid sequences of DNA ligases indicates that there is a high level of sequence conservation between the various known ligases. The level of sequence similarity between the corresponding part of sequence set forth in SEQ ID NO:16 and the consensus sequence set forth in known DNA ligases is 95%.

Based on the result of the homology described with respect to the consensus sequence, the specification asserts that SEQ ID NO:15 encodes a DNA ligase.

[Result of the prior art search]
The prior art search did not identify any sequence with over 40% similarity to the nucleotide sequence set forth in SEQ ID NO:15 or the amino acid sequence of SEQ ID NO:16.
It is a common general technological knowledge that DNA ligases have a well-established utility.

Case 9

[Claim 1] An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:17.

[Description of the invention]
The claimed polynucleotide is a 2700bp cDNA obtained from a human liver cDNA library.
It encodes a full-length protein of 800 amino acids of SEQ ID NO:18.
A similarity search was performed using a known DNA and amino acid database. The claimed polynucleotide showed 90% homology to the polynucleotide encoding a factor XX1 described in prior art document A. The amino acid sequence set forth in SEQ ID NO:18 showed 95% homology to a rat factor XX1 as described in prior art document A.
Based on the result of the similarity search, the specification asserts that the claimed polynucleotide encodes a human factor XX1, and may be used to treat patients having a disease or condition related to a factor XX1. No specific disease or condition that is related to a factor XX1 is disclosed.

[Result of the prior art search]
The prior art search did not identify any sequence with over 50% similarity to the nucleotide sequence set forth in SEQ ID NO:17 or the amino acid sequence of SEQ ID NO:18 other than that the rat polynucleotide encoding rat factor XX1 or the amino acid sequence of rat factor XX1.
It is a well known that mammalians including humans have factor XX1.
It is a common general technological knowledge that factor XX1 has a well-established utility.

Case 10

[Claim 1] An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:19.

[Description of the invention]
The claimed polynucleotide is a 2400bp cDNA obtained from a human liver cDNA library.
It encodes a full-length protein of 800 amino acids of SEQ ID NO:20.
A similarity search was performed, and the claimed polynucleotide was found to have 80% homology to a polynucleotide encoding a DNA ligase. An aligment of SEQ ID NO:20 with known amino acid sequences of DNA ligases indicates that there is a high level of sequence conservation between the various known ligases. The overall level of sequence similarity between SEQ ID NO:20 and consensus sequence set forth in known DNA ligases is 95%. The similarity search also confirms that SEQ ID NO:19 has high homology to nucleic acids that encode DNA ligases.
Based on the result of the homology described with respect to the consensus sequence, the specification asserts that SEQ ID NO:19 encodes a DNA ligase.

[Result of the prior art search]

The next highest level of homology is to alpha-actin and the homology is 50%.

It is a common general technological knowledge that DNA ligases have a well-established utility.

Answer (Basic question)

USPTO

1. Under 35 U.S.C. § 101, a product, process, manufacture, or composition of matter is patent eligible subject matter. The USPTO treats nucleic acid molecules as chemical compounds (compositions of matter). Nucleic acid molecules are comprised of nucleotide subunits arranged in a linear order that, in some circumstances, bestows functionality upon the molecule when used in the appropriate context. The information content of a molecule is viewed as one of its properties.

2. In order to comply with the utility requirement (35 U.S.C. § 101), an invention must be supported by a specific, substantial, and credible utility. A specific, substantial, and credible utility must either be disclosed in the as-filed specification, or be well-established. A well-established utility (that is, a specific, substantial, and credible utility that a person skilled in the art would immediately appreciate) need not be particularly disclosed within the body of the specification as long as it would have been well known, immediately apparent, or implied by the specification's disclosure of the properties of the disclosed nucleic acid, alone or taken with the knowledge of one skilled in the art.

3. As noted above in response to Question 2, in order to meet the utility requirement, each claimed invention must be supported by a specific, substantial, or credible utility, or a well-established utility.

   A utility is considered to be *specific* when it is particular to the subject matter disclosed, in contrast to a *general* utility that would be applicable to the broad class of the invention.

   A utility is considered to be *substantial* when it defines a "real world" use. However, disclosed utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

   An assertion of a specific and substantial utility is considered to be *credible* unless the logic underlying the assertion is seriously flawed (e.g., the assertion is based on theories that are contradictory to well-established principles, such as the first law of thermodynamics or the conservation of momentum), or the facts upon which the assertion is based are inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. A *credible* utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use.

   The test for enablement is whether one skilled in the art can make and use the invention based upon the disclosure present in the application coupled with information known in the art without undue experimentation. Factors to be considered when determining whether a disclosure satisfies the enablement requirement include the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the level of predictability in the art, the amount of direction provided by the inventor(s), the existence of any working examples, and the quantity of experimentation needed to make or use the

invention based on the content of the disclosure. This analysis is set forth in the decision of the Court of Appeals for the Federal Circuit in *In re Wands,* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

4. The USPTO does not have any *ab initio* requirement for experimental evidence to demonstrate the function or utility of any invention. However, where the Office has established a *prima facie* case of unpatentability for failure to comply with the utility and/or enablement requirements, the burden of proof shifts to applicant to rebut the *prima facie* case. Applicants may choose to submit experimental evidence or documentary evidence to support their assertions with respect to utility or enablement.

EPO

1. According to EPO practice, a claim to a nucleic acid molecule is a product claim to biological material (compound).

2. For the EPO the function of a claimed sequence is sufficiently disclosed when the information on the function given in the application allows a meaningful conclusion on how the sequence can be exploited, i.e. made and used, industrially (Article 57 and Rules 23(e)(3) and 27(1)(f)EPO) in the case of nucleic acid-related inventions this is usually a pharmacologically exploitable or a regulatory function. Accordingly, the function performed by a claimed sequence and the protein it encodes should be certain to the degree that a specific utility for the sequence becomes apparent beyond the realm of speculation. General statements ("throw-away utility") regarding the function are insufficient for these purposes.

3. Article 57 and Rules 23(e)(3) and 27(1)(f) of the EPC specify that an invention must be industrially exploitable , in the sense that it can be made and used in industry .The enablement requirement (Article 83 and Rule 27 (1)(e) EPC) specifies that the skilled person must be enabled to carry out the invention. For nucleic acid-related sequences this is interpreted to mean that the skilled person must be enabled to reproduce the invention and put it to work, i.e. industrially exploit it. This is typically achieved by the use of examples where appropriate (Rule 27(e) EPC). Depending on the scope of a claim, additional examples may be required if one example is not enough. In any event mere speculation and predictions based on similarity with a sequence of a known function are mostly not sufficient. Accordingly, claims on proteins encoded by nucleotide sequences that have not even been expressed in a host (typically a bacterial, yeast or animal cell line) are very likely not to satisfy the enablement requirement for the same reasons that cannot satisfy the requirement for industrial application. Therefore in the context of the following specific examples emphasis is put on assessment of industrial application rather than enablement.

4. If the alleged function of a claimed nucleic acid molecule is not credible beyond mere speculation the EPO will request experimental evidence demonstrating the function in accordance with Rule 27(e) EPC. Supplementary technical information providing evidence must be filed by the applicant upon request. Such evidence, although not formally part of the description, will be taken into account when assessing patentability. Experimental evidence normally is a prerequisite for second medical use claims.

JPO

1.The JPO treats it as a compound.

2.The JPO requires a function from which we can assume the specific utility (the specific function) or the specific function recognized from the common general knowledge as of the filing.

3.The JPO thinks that the applicants should show the information which can indicate the claimed polynucleotide probably encodes a certain functional protein. (Ex. Experiment results : High similarity to an already known protein which has a specific function)

4.The JPO requests experimental identification when the claimed polynucleotide is not proved as encoding a certain functional protein by written argument or from the common general knowledge as of the filing.

Answers (Hypothetical cases)

USPTO

Case 1

Utility (Industrial applicability): No

In order to comply with the utility requirement of 35 U.S.C. §101, claimed subject matter must be supported by a disclosure of a specific, substantial, and credible utility or by a well-established utility. In the instant case, the only information available pertaining to the claimed polynucleotide is its sequence and the fact that it was obtained from a liver cDNA library. The only asserted utility is the use of the nucleic acid in drug screening assays. This utility would not be considered to be specific because any nucleic acid could be used to screen for some sort of pharmaceutical agent. The utility would not be considered to be substantial because in the absence of particular information regarding the nature of the nucleic acid or the putative protein encoded by the nucleic acid, one skilled in the art would need to perform further experimentation on the material itself in order to determine what conditions any drugs found using the claimed nucleic acids or protein encoded thereby would have been useful for. In addition, since the claimed nucleic acid is novel, no well-established utility that would be provided by the extant knowledge in the art is evident.

Enablement requirement: No

In order to comply with the enablement requirement of 35 U.S.C. §112, first paragraph, a specification must disclose how to make and use the claimed subject matter for at least one specific, substantial, and credible utility. In the instant case, the fact pattern under consideration fails to provide any specific and substantial utility for the claimed invention. Therefore, the disclosure would not have taught one skilled in the art how to use the invention without undue experimentation.

Inventive step (Non-obviousness): Yes

The claim is limited to a specific nucleic acid sequence (SEQ ID NO: 1). The facts in this case indicate that no sequences present in the prior art anticipate the nucleic acid sequence. The closest prior art sequence had no more than 30% similarity to the claimed sequence. In order to establish a *prima facie* case of obviousness, the examiner would have to establish that one of ordinary skill in the art would have been motivated to isolate the claimed nucleic acid from the same source as applicant especially in view of the degeneracy of the genetic code, and given that the general state of the prior art indicates that even nucleic acids encoding the same protein may vary based upon their origin. "A general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out." *In re Deuel*, 51 F.3d 1552, 1558, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995). The fact that a general process can be conceived in advance for preparing an undefined compound does not mean that a specifically claimed compound could have been precisely envisioned and therefore obvious. Since the state of the molecular biology art indicates that there may be significant nucleic acid sequence polymorphisms between molecules that encode the same proteins, unless the prior art would have led one to have isolated a nucleic acid with the same sequence as claimed, the examiner could not establish a *prima facie* case of obviousness. Therefore on the facts of this case, the claimed nucleic acids would

not have been considered obvious to one of ordinary skill in the art at the time the invention was made.

Case 2

Utility (Industrial applicability): No

In order to comply with the utility requirement of 35 U.S.C. §101, claimed subject matter must be supported by a disclosure of a specific, substantial, and credible utility or by a well-established utility. In the instant case, the claimed nucleic acid encodes a protein that includes a DNA-binding motif. The presence of a given motif within a protein sequence does not necessarily establish by a preponderance of the evidence (i.e. does not make it more likely than not) that the protein would, in fact, have the function associated with the motif. The examination process must include a critical analysis of the significance of any given motif and its implication in a protein's function. Therefore, the first question that needs to be addressed is whether or not the claimed nucleic acid actually encodes a DNA-binding protein. If one skilled in the art would accept that the presence of a DNA-binding motif within an otherwise novel protein would have been sufficient to support the assertion that the novel protein actually bound DNA nonspecifically, then the question of utility would stand or fall on whether or not a specific, substantial and credible use for this binding activity was set forth in the specification or was well established in the art. In the instant case, no specific use for DNA binding proteins is disclosed or is well established in the art. Although the specification asserts that the protein of SEQ ID NO: 4 could be used in drug screening assays, such an assertion would not be considered to be a specific, substantial, or credible utility for reasons set forth above in the **Case 1** analysis. Therefore, even were it accepted that the claimed nucleic acid encoded a DNA binding protein, this would not suffice to support a specific, substantial, and credible utility.

In addition, it is noted that the both the similarity search set forth in the description of the invention as well as the prior art search indicate a homology level of no greater than 30% as compared with the prior art, thus, potentially, other proteins unrelated to DNA-binding proteins would be as similar to SEQ ID NO: 4 as to DNA-binding proteins. Therefore, there would be sufficient evidence to question whether SEQ ID NO: 4 is a DNA binding protein.

Enablement requirement: No

In order to comply with the enablement requirement of 35 U.S.C. §112, first paragraph, a specification must disclose how to make and use the claimed subject matter for at least one specific, substantial, and credible utility. In the instant case, the fact pattern under consideration fails to provide any specific and substantial utility for the claimed invention. Therefore, the disclosure would not have taught one skilled in the art how to use the invention without undue experimentation.

Inventive Step (non-obviousness): Yes

The claim is limited to a specific nucleic acid sequence (SEQ ID NO: 3). The facts in this case indicate that no sequences present in the prior art anticipate the claimed invention. The closest prior art sequence had a DNA binding motif, but had no more than 30% similarity to the claimed sequence. For the reasons set forth in the analysis of **Case 1**, in the absence of any prior art disclosure leading one of ordinary skill in the art to select the particularly claimed nucleic acid, the claimed invention would not have been obvious.

Case 3

Utility (Industrial applicability): Case by case

In order to comply with the utility requirement of 35 U.S.C. §101, claimed subject matter must be supported by a disclosure of a specific, substantial, and credible utility or by a well-established utility. In the instant case, the claimed nucleic acid encodes a protein that includes a VV1 motif that is indicative of the potential of said nucleic acid to actually encode a factor VV1. However, the presence of a given motif within a protein sequence does not establish by a preponderance of the evidence (i.e. does not make it more likely than not) that the protein would, in fact, have the function associated with the motif, i.e, that the protein would have been a factor VV1. Therefore, the first question that needs to be addressed is whether or not the claimed nucleic acid actually encodes a factor VV1. If one skilled in the art would accept that the presence of a VV1 motif within an otherwise novel protein would have been sufficient to support the assertion that the novel protein is a factor VV1, then the claimed invention would comply with the utility requirement of 35 U.S.C. § 101 because the claimed nucleic acid would encode a factor VV1, and factor VV1 has a well established utility (as set forth in the fact pattern). If the art did not provide such a nexus, then the assignment of the protein encoded by SEQ ID No. 5 as a factor VV1 would not be sufficient to support a specific, substantial, and credible utility.

With regard to the assertion that the protein of SEQ ID NO: 6 could be used in drug screening assays, such an assertion would not be considered to be a specific, substantial, or credible utility for reasons set forth above in the **Case 1** analysis.

In addition, it is noted that the both the similarity search set forth in the description of the invention as well as the prior art search indicate a homology level of no greater than 30%. Potentially, other proteins unrelated to factor VV1 proteins would be as similar to SEQ ID NO: 6 as VV1 proteins, and the assignment of SEQ ID NO: 6 as a VV1 protein could be questioned. However, the fact pattern at issue particularly states that SEQ ID NO: 6 contains a factor VV1 motif and no evidence is set forth to rebut this proposition.

Enablement requirement: Case by case

As noted above, there are two potential utilities that applicant might rely upon in **Case 3**, a well-established utility based upon SEQ ID NO:6 being a factor VV1 and its use in drug screening assays.

If SEQ ID NO: 6 were accepted to be a factor VV1, it would have a well established utility that would be enabled based upon extant knowledge in the art.

If SEQ ID NO: 6 were not accepted as being a factor VV1, it would not be considered to be enabled for how to use for reasons set forth in the response to **Case 1** above.

Inventive Step (non-obviousness): Yes

The claim is limited to a particular nucleic acid sequence (SEQ ID NO: 5). The facts in this case indicate that no sequences present in the prior art anticipate the claimed invention. In the absence of a prior art disclosure teaching that additional proteins having a factor VV1 are expected to exist, and absent a motivation to look for other factor VV1 encoding nucleic acids in the same source material as that used

by applicant, SEQ ID NO: 5 would have been considered nonobvious. See the analysis set forth with respect to **Case 1.**

Case 4

Utility (Industrial applicability): Yes

In order to comply with the utility requirement of 35 U.S.C. §101, claimed subject matter must be supported by a disclosure of a specific, substantial, and credible utility or by a well-established utility. In the instant case, the claimed nucleic acid is asserted to encode a human factor UU1 protein. The results of the prior art search indicate that if a protein is accepted as being a factor UU1 protein, it would have a well established utility.

The instant fact pattern sets forth two potential utilities. The first is the use of the putatively encoded protein in the treatment of unspecified diseases or conditions and the second is a possible well established utility based upon extant knowledge in the art.

With regard to the use of the proteins to treat unspecified diseases or conditions, since any protein may potentially be used as a treatment agent, this utility would not be considered to be specific. Since no particular disease or condition is disclosed, one skilled in the art would have to perform additional experimentation to identify and/or reasonably confirm the asserted use as a treatment agent and therefore, this utility would not be considered to be substantial.

With regard to a well established utility for a human factor UU1, while the stated level of similarity both within the specification and as revealed by the prior art search indicates a low level of sequence identity (30%), the fact pattern specifically states that structural information would have supported a conclusion by one skilled in the art that the protein of SEQ ID NO: 8 would be a factor UU1. In addition, the prior art search indicates that a factor UU1 would have a well established utility. Therefore, since the fact pattern at issue does not provide any reason to doubt that the nucleic acid of SEQ ID NO: 7 encodes a factor UU1 and such have well established utility on this record, the nucleic acid of SEQ ID NO: 7 would comply with the utility requirement based on its ability to encode the factor UU1 protein of SEQ ID NO: 8.

Enablement requirement: Yes

As noted above, there is no reason to question that SEQ ID NO: 8 is a human UU1 protein and such proteins have well established utilities. As such, given an UU1 protein, the skilled artisan would have been able to have used the claimed nucleic acid to prepare a human factor UU1 and to have used this factor in a manner supported by extant knowledge in the art.

Inventive Step (non-obviousness): Yes

The claim is limited to a particular nucleic acid sequence (SEQ ID NO: 7). The facts in this case indicate that no sequences present in the prior art anticipate the claimed invention. In the absence of a prior art disclosure teaching that additional proteins having a factor UU1 are expected to exist, and absent a motivation to look for other factor UU1 encoding nucleic acids in the same source material as that used by applicant, SEQ ID NO:7 would have been considered nonobvious. See the analysis in **Case 1.**

Case 5

Utility (Industrial applicability): No

In order to comply the utility requirement of 35 U.S.C. §101, claimed subject matter must be supported by a disclosure of a specific, substantial, and credible utility or by a well-established utility. In the instant case, the claimed nucleic acid is asserted to encode a protein that is a member of a family of related proteins. The results of the prior art search indicate that while individual members of this family of proteins may have well established uses, no utility of an individual member of the protein family may be assigned *a priori*.

The instant fact pattern sets forth two potential utilities. The first is the use of the putatively encoded protein in the treatment of unspecified diseases or conditions, and the second is a possible well established utility based upon extant knowledge in the art. However, with regard to the second potential utility, the fact pattern specifically indicates that there is no well established use for each individual member of the indicated family of proteins. Therefore, the claimed nucleic acid would not have a well-established utility.

With regard to the use of the proteins to treat diseases or conditions associated with the disclosed family of proteins, the facts at issue fail to disclose what such diseases or conditions would be. Since any protein may potentially be used as a treatment agent, this utility would not be considered to be specific. Since no particular disease or condition is disclosed, the artisan would have been required to perform additional experimentation to identify and/or reasonably confirm the asserted use as a treatment agent and therefore, this utility would not be considered to be substantial.

Enablement requirement: No

Since there is no specific, substantial, and credible or well established utility for the claimed nucleic acid or the protein encoded thereby, one skilled in the art would not have been able to use the claimed invention without undue experimentation. In addition, it is noted that even if the specification disclosed a particular disease or condition that could potentially have been treated using the protein of SEQ ID NO: 10, supporting information would have been needed in regard to how the protein would be used in any particular treatment regimen.

Inventive Step (non-obviousness): Yes

The claim is limited to a particular nucleic acid sequence (SEQ ID NO: 9). The facts in this case indicate that no sequences present in the prior art anticipate the claimed invention. In the absence of a prior art disclosure teaching that additional proteins of the recited family of proteins are expected to exist, and absent a motivation to look for other nucleic acids encoding other members of the family of proteins in the same source material as that used by applicant, SEQ ID NO:9 would have been considered nonobvious. See the analysis set forth in **Case 1.**

Case 6

Utility (Industrial applicability): No

In order to comply with the utility requirement of 35 U.S.C. §101, claimed subject

matter must be supported by a disclosure of a specific, substantial, and credible utility or by a well-established utility. In the instant case, the claimed nucleic acid is asserted to encode a human factor YY1 protein. The results of the prior art search indicate that if a protein is accepted as being a factor YY1 protein, it would have a well established utility.

The instant fact pattern sets forth two potential utilities. The first is the use of the putatively encoded protein in the treatment of unspecified diseases or conditions and the second is a possible well established utility based upon extant knowledge in the art.

With regard to the use of the proteins to treat diseases or conditions associated with the disclosed family of proteins, the facts at issue fail to disclose what such diseases or conditions would be. Since any protein may potentially be used as a treatment agent, this utility would not be considered to be specific. Since no particular disease or condition is disclosed, the artisan would have been required to perform additional experimentation to identify and/or reasonably confirm the asserted use as a treatment agent and therefore, this utility would not be considered to be substantial.

With regard to a well established utility for a human factor YY1 protein, the question to be addressed is whether or not the nucleic acid of SEQ ID NO: 11 would encode a factor YY1. The application at issue discloses a 55% homology at the nucleic acid or protein level to factor YY1 of rat, and a search of the prior art revealed a 45% homology to factor YY2 of pig, and a 40% homology to a factor YY3 of monkey. Neither the specification nor the prior art disclose any information regarding the evolutionary significance of these homologies or relative conservation of structure and function across species. For example, there is no evidence of record showing why homology to a rodent sequence would provide a better basis for assigning protein function than homology to a primate species. Given the above information, and in light of the art recognized fact that minor sequence differences can significantly affect a protein's function, one skilled in the art would find it more likely than not that SEQ ID NO: 12 is not a human factor YY1. Since there is a significant question as to whether SEQ ID NO: 12 was a factor YY1, the applicant could not rely upon a well established utility for the claimed nucleic acid encoding the protein of SEQ ID NO: 14.

Enablement requirement: No

Since there is no specific, substantial, and credible or well established utility for the claimed nucleic acid or the protein encoded thereby, the artisan would not have been able to have used the claimed invention without undue experimentation. In addition, it is noted that even were the specification to have disclosed a particular disease or condition that could potentially have been treated using the protein of SEQ ID NO: 12, supporting information would have been needed in regard to how the protein would be used in any particular treatment regimen.

Inventive Step (non-obviousness): Yes

The claim is limited to a particular nucleic acid sequence (SEQ ID NO: 11). The facts in this case indicate that no sequences present in the prior art anticipate the claimed invention. In the absence of a prior art disclosure teaching that human proteins having a factor YY1 are expected to exist, and absent a motivation to look for human factor YY1 encoding nucleic acids in the same source material as that used by applicant, SEQ ID NO: 11 would have been considered nonobvious. See the analysis set forth in **Case 1.**

Case 7

Utility (Industrial applicability): No

In order to comply with the utility requirement of 35 U.S.C. §101, claimed subject matter must be supported by a disclosure of a specific, substantial, and credible utility or by a well-established utility. In the instant case, the claimed nucleic acid is asserted to encode a human factor WW1 protein. The results of the prior art search indicate that if a protein is accepted as being a factor WW1 protein, it would have a well established utility.

The instant fact pattern sets forth two potential utilities. The first is the use of the putatively encoded protein in the treatment of unspecified diseases or conditions and the second a possible well established utility based upon extant knowledge in the art.

With regard to the use of the proteins to treat diseases or conditions associated with the disclosed family of proteins, the facts at issue fail to disclose what such diseases or conditions would be. Since any protein may potentially be used as a treatment agent, this utility would not be considered to be specific. Since no particular disease or condition is disclosed, the artisan would have been required to perform additional experimentation to identify and/or reasonably confirm the asserted use as a treatment agent and therefore, this utility would not be considered to be substantial.

With regard to a well established utility for a human factor WW1 protein, the question to be addressed is whether or not the nucleic acid of SEQ ID NO: 13 would encode a factor WW1. The application at issue discloses only a 20-30% similarity at the nucleic acid or protein level while the prior art search does not identify any sequence with over 40% similarity to SEQ ID NO: 13. Furthermore, there is no information pertaining to the significance of the percent similarity, e.g., whether there were any conserved motifs that would have led the artisan to accept the protein's function. Given the above information, and in light of the art recognized fact that minor sequence differences can significantly affect a protein's function, one skilled in the art would find it more likely than not that SEQ ID NO: 14 is not a human factor WW1.

Since there is a substantial question as to whether SEQ ID NO: 14 was a factor WW1, the applicant could not rely upon a well established utility for the claimed nucleic acid encoding the protein of SEQ ID NO: 14.

Enablement requirement: No

Since there is no specific, substantial, and credible or well established utility for the claimed nucleic acid or the protein encoded thereby, the artisan would not have been able to have used the claimed invention without undue experimentation. In addition, it is noted that even were the specification to have disclosed a particular disease or condition that could potentially have been treated using the protein of SEQ ID NO: 14, supporting information would have been needed in regard to how the protein would be used in any particular treatment regimen.

Inventive Step (non-obviousness): Yes

The claim is limited to a particular nucleic acid sequence (SEQ ID NO: 13). The

facts in this case indicate that no sequences present in the prior art anticipate the claimed invention. In the absence of a prior art disclosure teaching that proteins having a human factor WW1 are expected to exist, and absent a motivation to look for human factor WW1 encoding nucleic acids in the same source material as that used by applicant, SEQ ID NO: 13 would have been considered nonobvious. See the analysis set forth in **Case 1.**

Case 8

Utility (Industrial applicability): Case by case

In order to comply with the utility requirement of 35 U.S.C. §101, claimed subject matter must be supported by a disclosure of a specific, substantial, and credible utility or by a well-established utility. In the instant case, the claimed nucleic acid is asserted to encode a DNA ligase. The results of the prior art search indicate that if a protein is accepted as being a DNA ligase, it would have a well established utility.

The disclosure does not assert any utility for the claimed nucleic acid other than as encoding a DNA ligase. Thus the question to be addressed is whether or not the nucleic acid of SEQ ID NO: 15 would encode a DNA ligase. The application at issue discloses an overall 30% sequence similarity to a polynucleotide encoding a DNA ligase, but a 95% similarity to the consensus sequence in known ligases. The prior art search indicates that prior art databases do not contain sequences with over 40% sequence identity to the claimed invention. If one skilled in the art would have considered the presence of the part of the sequence that is 95% homologous to known DNA ligases to be sufficient to establish that SEQ ID NO: 16 is a DNA ligase, then the claimed invention has a well-established utility. If, however, one skilled in the art would merely consider the consensus sequence to be indicative of conserved domains in DNA ligases, but not to be dispositive of the assignment of a given protein *as* a DNA ligase, then there is a reason to question whether SEQ ID NO: 16 is a DNA ligase, especially given the fact that the prior art search revealed potentially unrelated sequences having a similar level of homology to the claimed sequence.

Enablement requirement: Case by case.

As noted above, if there is no reason to question that SEQ ID NO: 16 encodes a DNA ligase, then the enablement requirement has been met because one skilled in the art would have been able to have used the claimed nucleic acid to prepare a DNA ligase and to have used this DNA ligase in a manner supported by extant knowledge in the art.

If, however, the disclosure is not sufficient to support the assertion that SEQ ID NO: 15 encodes a DNA ligase, then the specification does not enable one skilled in the art to use the claimed invention without undue experimentation because there is no specific, substantial, and credible utility for the claimed invention.

Inventive Step (non-obviousness): Yes

The claim is limited to a particular nucleic acid sequence (SEQ ID NO: 15). The facts in this case indicate that no sequences present in the prior art anticipate the claimed invention. In the absence of a prior art disclosure teaching that other DNA ligases are expected to exist, and absent a motivation to look for DNA ligases in the same source material as that used by applicant, SEQ ID NO: 15 would have been

considered nonobvious. See the analysis set forth in **Case 1.**

Case 9

Utility (Industrial applicability): Yes

In order to comply with the utility requirement of 35 U.S.C. §101, claimed subject matter must be supported by a disclosure of a specific, substantial, and credible utility or by a well-established utility. In the instant case, the claimed nucleic acid is asserted to encode a human factor XX1 protein. The results of the prior art search indicate that if a protein is accepted as being a factor XX1 protein, it would have a well established utility.

The instant fact pattern sets forth two potential utilities. The first is the use of the putatively encoded protein in the treatment of unspecified diseases or conditions and the second is a possible well established utility based upon extant knowledge in the art.

With regard to the use of the proteins to treat diseases or conditions associated with the disclosed family of proteins, the facts at issue fail to disclose what such diseases or conditions would be. Since any protein may potentially be used as a treatment agent, this utility would not be considered to be specific. Since no particular disease or condition is disclosed, the artisan would have been required to perform additional experimentation to identify and/or reasonably confirm the asserted use as a treatment agent and therefore, this utility would not be considered to be substantial.

With regard to a well established utility for a human factor XX1 protein, the question to be addressed is whether or not the nucleic acid of SEQ ID NO: 18 would encode a factor XX1. The application at issue discloses a 90% sequence similarity at the nucleic acid level and a 95% similarity at the protein level while the prior art search indicates that prior art databases do not contain sequences with over 50% sequence identity. Given this information, there is no reason to doubt that the claimed nucleic acid of SEQ ID NO: 17 encodes a human factor XX1 protein. Since factor XX1 proteins have well established uses, the nucleic acid of SEQ ID NO: 17 would have a well established utility in so far as it would be expected to encode a human factor XX1.

Enablement requirement: Yes

As noted above, there is no reason to question that SEQ ID NO: 18 is a human XX1 protein and such proteins have well established utilities. As such, given an XX1 protein, the artisan would have been able to have used the claimed nucleic acid to prepare a human factor XX1 and to have used this factor in a manner supported by extant knowledge in the art.

Inventive Step (non-obviousness): Yes

The claim is limited to a particular nucleic acid sequence (SEQ ID NO: 17). The facts in this case indicate that no sequences present in the prior art anticipate the claimed invention. In the absence of a motivation to look for human factor XX1 encoding nucleic acids in the same source material as that used by applicant, SEQ ID NO: 17 would have been considered nonobvious. See the analysis set forth in **Case 1.**

Case 10

Utility (Industrial applicability): Yes

In order to comply with the utility requirement of 35 U.S.C. §101, claimed subject matter must be supported by a disclosure of a specific, substantial, and credible utility or by a well-established utility. In the instant case, the claimed nucleic acid is asserted to encode a DNA ligase. The results of the prior art search indicate that if a protein is accepted as being a DNA ligase, it would have a well established utility.

The disclosure does not assert any utility for the claimed nucleic acid other than as encoding a DNA ligase. Thus the question to be addressed is whether or not the nucleic acid of SEQ ID NO: 19 would encode a DNA ligase. The application at issue discloses an overall 80% sequence similarity to a polynucleotide encoding a DNA ligase, and a 95% similarity to the consensus sequence in known ligases. Further, the prior art search indicates that the closest non-ligase prior art sequence is an alpha-actin with 50% homology to the claimed invention. Given the overall level of sequence similarity and the high level of conservation of consensus sequences consistent with the assignment of a protein as a DNA ligase, based on the facts in this case it would have been more likely than not that applicant's assertion is correct. Thus, one skilled in the art would accept the assertion that the nucleic acid of SEQ ID NO: 19 encodes a DNA ligase. Finally, since DNA ligases have well established uses, the nucleic acid of SEQ ID NO: 19 would have a well established utility in so far as it would be expected to encode a DNA ligase.

Enablement requirement: Yes

As noted above, one skilled in the art would accept the assertion that SEQ ID NO: 20 is a DNA ligase, and the record establishes that such proteins have well established utilities. As such, given a DNA ligase, one skilled in the art would have been able to use the claimed nucleic acid to prepare a DNA ligase and to use the DNA ligase in a manner supported by extant knowledge in the art.

Inventive Step (non-obviousness): Yes

The claim is limited to a particular nucleic acid sequence (SEQ ID NO: 19). The facts in this case indicate that no sequences present in the prior art anticipate the claimed invention. In the absence of a prior art disclosure teaching that additional DNA ligases are expected to exist, and absent a motivation to look for DNA ligases in the same source material as that used by applicant, SEQ ID NO: 19 would have been considered nonobvious. See the analysis set forth in Case 1.

EPO

Case 1

Industrial application: No

In light of the complete lack of any information on the function of the isolated sequence can be commercially exploited is neither apparent nor inferable (Article 57, Rules 23 (e)(3) and 27(1)(f) EPC).

Inventive step: No

In the absence of a specific technical effect of a claimed human cDNA, any and all previously known human cDNAs are considered as prior art for the assessment of inventive step. In such a case the only technical problem solved by the claimed polynucleotide is the mere provision of further human cDNAs, regardless of their likely useful properties. An arbitrary choice of a cDNA obtained through a routine cloning exercise cannot involve an inventive step because it is not justified by a technical purpose.

Case 2

Industrial Application: No

The presence of a DNA binding motif in a protein is not a true indication of what function the protein really performs. Therefore the same reasoning as in Case 1 applies.

Inventive step: No
see Case 1

Case 3

Industrial Application: No
The presence of a factor VV1 motif in a protein is not a true indication that the protein performs the function of VV1. Therefore the same reasoning as in Case 1 applies.

Inventive step: No
see Case 1

Case 4

Industrial Application: Case by case

Given that the similarity of the newly isolated sequences to known sequences is below 30%, the additional technical information becomes crucial. If only structural information is provided then the function still remains merely speculative and the industrial application has to be denied for the reasons given under Case 1.

Inventive step: Case by case

If it were known in the art that factor UU1 has a human homolog (ortholog) and that the factor UU1 motif is essential for factor UU1 functioning, then it would have been obvious for the skilled person to design primers from the motif region and thus clone factor UU1 from a human cDNA library. In such a case, inventive step would be denied.

Case 5

Industrial Application: No
The definition of a protein as belonging to a certain family does not infer a certain function on that protein. Therefore same reasoning as for Case 1 applies.

Inventive step: No
see Case 1

Case 6

Industrial Application: No

The homology of 55% to rat factor YY1 is too low to allow a credible assignment of the function of YY1 to the newly isolated protein. The function requirement is therefore not satisfied and the same reasoning as in Case 1 applies.

Inventive step: No

see Case 1 and Case 4

Case 7

Industrial Application: No

A 20-30% homology to rat factor WW1 is too low to allow a credible assignment of the function of factor WW1 to the newly isolated protein. The function requirement is therefore not satisfied and the same reasoning as in Case 1 applies.

Inventive step: No

see Case 1 and Case 4

Case 8

Industrial Application: No

A 30% overall homology to DNA ligases is too low, even if the homology to the consensus is 95%. In that case the function of the newly isolated sequence is based on mere speculation failing to satisfy the utility requirement.

Inventive step: No
It is known in the art that several DNA ligases exist that share a consensus sequence. It is thus obvious for the skilled person to design generate primers from

the consensus sequence and thus clone further DNA ligases from a human cDNA library.

Case 9

Industrial Application: Yes

In the present case the EPO would recognise that the newly isolated sequence encodes human factor XX1 that has a well established utility in the art.

Inventive step: No

It is well known in the art that mammalians including humans have factor XX1 orthologs. It would have been obvious for the skilled person to design primers to clone factor XX1 from a human cDNA library.

Case 10

Industrial Application: Yes

In the present case the EPO would recognise that the newly isolated sequences encodes a DNA ligase that has a well established utility in the art.

Inventive step: No

It is known in the art that several DNA ligases exist that share a consensus sequence and thus clone further DNA ligases from a human cDNA library.

JPO

Case 1

Utility (Industrial applicability): No

Where subject matter of an invention is commercially applicable, the invention is considered to meet the industrial applicability requirement.

As utility of the claimed polynucleotide is not described in the specification or cannot be inferred, the claimed invention is not commercially applicable, thus, does not meet the requirements set forth in the first sentence in Section 29(1) of the Patent Law.

Enablement requirement: No

For an invention of a product, the invention shall be described so as to enable to make and to use the product in an industrially applicable way. (except in cases where the product could be made and used by a person skilled in the art without such explicit description when taking into account the overall descriptions of the specification, drawings and the common general knowledge as of the filing.)

In Case 1, there is a description that "An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:1" encodes a novel protein and may be used in drug screening assays. However, there is no description of the function of the protein encoded by the claimed polynucleotide. Moreover, the specific function of that protein cannot be assumed from the common general knowledge as of the filing. As the specific function of the claimed polynucleotide is not clear and it is not clear how to use the claimed polynucleotide.

As there is no disclosure concerning the use of the claimed polynucleotide, the description of the invention is deemed insufficient for enabling a person skilled in the art to carry out the invention.

(Attention)
The words "the specific function" mean the function from which we can assume the specific utility in the JPO's answer.

Inventive Step: Yes

Obtaining cDNAs from human cells is a well-known activity.

However, the mere publicity of the polynucleotide which has low similarity to the polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:1 is not sufficient reason to demonstrate that it is easy to obtain the claimed polynucleotide.

Case 2

Utility (Industrial applicability): No

As utility of the claimed polynucleotide is not described in the specification or cannot be inferred, the claimed invention is not commercially applicable.

Enablement requirement: No

In Case 2, there is a description that "An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:3" encodes a novel DNA-binding protein and may be used in drug screening assays. However, the reason given by the applicant why the protein set forth in SEQ ID NO:4 is a DNA-binding protein is that the claimed polynucleiotide includes a DNA-binding protein motif which is based only on the result of the motif search.

In general, it cannot be said necessarily that it is probable that the polypeptide had a DNA-binding activity in common only under the condition that the polypeptide includes a DNA-binding motif. Therefore, we do not consider directly that the protein which is encoded by the claimed polynucleotide has a DNA-binding activity based on the existence of a DNA-binding motif.

Moreover, the protein's specific function cannot be recognized as there are so many DNA-binding proteins whose specific functions differ.

The specific function of the claimed polynucleotide also cannot be assumed with the common general knowledge as of the filing. The specific function of the claimed polynucleotide is therefore not clear and it is not clear how to use the claimed polynucleotide.

Therefore, we consider there is no disclosure concerning the use of this polynucleotide in an industrial applicable way, thus the description of the invention is deemed insufficient for enabling a person skilled in the art to carry out the invention.

Inventive Step: Case by case

Obtaining cDNAs from human cells is a well-known activity.

However, the mere publicity of the polynucleotide which has low similarity to the polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:3 is not a sufficient reason to demonstrate that it is easy to obtain the claimed polynucleotide.

In general, an amino acid sequence forming a motif includes many indetermined amino acids. However, if the DNA-binding protein motif has a specific and successive amino acid sequence and it is possible to make a useful PCR primer for obtaining a polynucleotide encoding a DNA-binding protein based on the sequence, it is probably obvious that the claimed polynucleotide can be obtained using the primer. Therefore, we consider this invention cannnot be regarded as involving an inventive step.

Case 3

Utility (Industrial applicability): No

As utility of the claimed polynucleotide is not described in the specification or cannot be inferred, the claimed invention is not commercially applicable.

Enablement requirement: No

In Case 3, there is a description that "An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:5" encodes a factor

VV1 and may be used in drug screening assays. However, the reason given by the applicant why the protein set forth in SEQ ID NO:6 is a factor VV1 protein is that the protein, includes a factor VV1 motif which is based only on the result of the motif search.

In general, it cannot be said necessarily that it is probable that the polypeptide has a factor VV1 activity in common only under the condition that the polypeptide includes a factor VV1 motif. Therefore, we do not consider directly that the protein which is encoded by the claimed polynucleotide has a factor VV1 activity based on only the existence of a factor VV1 motif.

Moreover, the specific function of the claimed polynucleotide also cannot be assumed with the common general knowledge as of the filing. The specific function of the claimed polynucleotide is therefore not clear and it is not clear how to use the claimed polynucleotide.

In this regard, we consider there is no disclosure concerning the use of this polynucleotide in an industrial applicable way, thus the description of the invention is deemed insufficient for enabling a person skilled in the art to carry out the invention.

Inventive Step: Case by case

Obtaining cDNAs from human cells is a well-known activity.

However, the mere publicity of the polynucleotide which has low similarity to the polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:5 is not a sufficient reason to demonstrate that it is easy to obtain the claimed polynucleotide.

In general, an amino acid sequence forming a motif includes many indetermined amino acids. However, if the factor VV1 motif has a specific and successive amino acid sequence and it is possible to make a useful PCR primer for obtaining a polynucleotide encoding the factor VV1 based on the sequence, it is probably obvious that the claimed polynucleotide can be obtained using the primer. We consider this invention cannot therefore be regarded as involving an inventive step.

Case 4

Utility (Industrial applicability): Yes

Enablement requirement: Yes

In Case 4, there is a description that “An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:7” encodes a factor UU1 and may be used in drug screening assays. In general, it cannot be said necessarily that the polypeptide has a factor UU1 activity in common only under the polypeptide includes a factor UU1 motif.
However, in this case, the applicant presents a fact that the claimed polynucleiotide includes a factor UU1 motif which is based only on the result of the motif search and additional technical information obtained in silico (e.g., structural information) such that one skilled in the art would recognize that the protein of SEQ ID NO:8 is a factor UU1. We consider that the protein is probably a factor UU1, and that the

specific function of the claimed polynucleotide is clear as the UU1 factor has a specific function.

Therefore, we consider the description of the invention is deemed sufficient for enabling a person skilled in the art to carry out the invention without certified experiment results.

Inventive Step: Case by case

Obtaining cDNAs from human cells is a well-known activity.

However, the mere publicity of the polynucleotide which has low similarity to the polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:7 is not a sufficient reason to demonstrate that it is easy to obtain the claimed polynucleotide.

In general, an amino acid sequence forming a motif includes many indetermined amino acids. However, if the factor UU1 motif has a specific and successive amino acid sequence and it is possible to make a useful PCR primer for obtaining a polynucleotide encoding UU1 based on the sequence, it is probably obvious that the claimed polynucleotide can be obtained using the primer. Therefore, we consider this invention cannot be regarded as involving an inventive step.

Case 5

Utility (Industrial applicability): No

As utility of the claimed polynucleotide is not described in the specification or cannot be inferred, the claimed invention is not commercially applicable.

Enablement requirement: No

In Case 5, there is a description that "An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:9" encodes a human protein that is a member of the ZZ family and may be used in drug screening assays. However, the reason given by the applicant why the protein set forth in SEQ ID NO:6 is a member of the ZZ family is that the claimed polynucleiotide showed 40% ~50% homology to the polynucleotide encoding a family of related proteins designated A,B,...V,W which is based only on similarity search.

In general, when two polynucleotides (polypeptides) show a low similarity to each other, it is probable that the two polynucleotides (polypeptides) do not have any specific functions in common. Therefore, we do not consider directly that the protein which is encoded by the claimed polynucleotide has ZZ family activity based on only 40%-50% homology to the polynucleotide encoding proteins that are members of a ZZ family.

Also, the protein's specific function cannot be recognized as there are so many ZZ family proteins whose specific functions differ.

Moreover, the specific function of the claimed polynucleotide also cannot be assumed with the common general knowledge as of the filing. The specific function of the claimed polynucleotide is therefore not clear and it is not clear how to use the claimed polynucleotide.

Therefore, we consider there is no disclosure concerning the use of this polynucleotide in an industrial applicable way, thus the description of the invention is deemed insufficient for enabling a person skilled in the art to carry out the invention.

Inventive Step: Case by case

Obtaining a cDNA encoding a protein that is a member of the same family is a well-known activity.

However, the mere publicity of the polynucleotide which has a low similarity to the polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:9 is not sufficient reason to demonstrate that it is easy to obtain the claimed polynucleotide.

In general, the conditions of hybridization carried out by a person skilled in the art are strict. It is the common general knowledge as of the filing that various polynucleotides, except the desired one, are obtained if the conditions are loosened. We therefore consider it difficult to obtain the claimed polynucleotide even if there are polynucleotides which have 40-50% homology to the claimed polynucleotide and consider this invention as involving an inventive step.

However, if it is probably possible to obtain the polynucleotide encoding a protein which is a member of a ZZ family (e.g. A consensus sequence which has high similarity among already known proteins A-W or documents which disclose the consensus sequence can be found), we consider this invention may not be regarded as involving an inventive step.

Case 6

Utility (Industrial applicability): No

As utility of the claimed polynucleotide is not described in the specification or cannot be inferred, the claimed invention is not commercially applicable.

Enablement requirement: No

In Case 6, there is a description that "An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:11" encodes a human factor YY1 and may be used in drug screening assays. However, the reason given by the applicant why the protein set forth in SEQ ID NO:12 is a factor YY1 protein is that the claimed polynucleiotide showed 55% homology to the polynucleotide encoding a factor YY1 of a rat which is based only on the similarity search.

In general, when two polynucleotides (polypeptides) show a low similarity to each other, it is probable that two polynucleotides (polypeptides) do not have any specific functions in common. Therefore, we do not consider directly that the protein encoded by the claimed polynucleotide has factor YY1 activity based on only 55% homology to the polynucleotides encoding a factor YY1 of a rat. Moreover, in this case, the claimed polynucleotide showed 45% homology to a polynucleotide encoding a factor YY2 of a pig and 40% homology to a polynucleotide encoding a factor YY3 of a monkey. The protein's specific function cannot therefore be recognized as there is the possibility that the claimed polynucleotide encodes a factor YY2 of a pig or a factor YY3 of a monkey.

Moreover, as the specific function of the claimed polynucleotide also cannot be assumed with the common general knowledge as of the filimg, the specific function

of the claimed polynucleotide is not clear and it is not clear how to use the claimed polynucleotide.

We therefore consider there is no disclosure concerning the use of this polynucleotide in an industrial applicable way, thus the description of the invention is deemed insufficient for enabling a person skilled in the art to carry out the invention.

Inventive Step: Case by case

Obtaining a cDNA encoding a protein that is a member of the same family is a well-known activity.

However, the mere publicity of the polynucleotide which has a low similarity to the polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:11 is not sufficient reason to demonstrate that it is easy to obtain the claimed polynucleotide.

If it is probably possible to obtain the polynucleotide encoding a human factor YY1 (e.g. A consensus sequence which has high similarity among already known factor YY1 proteins, or documents which disclose consensus sequence, can be found. The case that we find a document which disclose the consensus sequence), we consider this invention may not be regarded as involving an inventive step.

Case 7

Utility (Industrial applicability): No

As utility of the claimed polynucleotide is not described in the specification or cannot be inferred, the claimed invention is not commercially applicable.

Enablement requirement: No

In Case 7, there is a description that "An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:13" encodes a human factor WW1 and may be used in drug screening assays. However, the given reason by applicant why the protein set forth in SEQ ID NO:14 is a factor WW1 protein is that the claimed polynucleiotide showed 20~30% homology to the polynucleotides encoding a factor WW1 of mammals which is only based on similarity search.

In general, when two polynucleotides (polypeptides) show a low similarity to each other, it is probable that two polynucleotides (polypeptides) do not have any specific functions in common. Therefore, we do not consider directly that the protein which is encoded by the claimed polynucleotide has the factor WW1 activity based on only the 20~30% homology to the polynucleotides encoding a factor WW1 of mammals.

Moreover, as the specific function of the claimed polynucleotide also cannot be assumed with the common general knowledge as of the filing, the specific function of the claimed polynucleotide is not clear and it is not clear how to use the claimed polynucleotide.

Therefore, we consider there is no disclosure concerning the use of this polynucleotide in an industrial applicable way, thus the description of the invention is deemed insufficient for enabling a person skilled in the art to carry out the invention.

Inventive Step: Case by case

Obtaining a cDNA encoding the same functional protein is a well-known activity.

However, only the publicity of the polynucleotide, which has a low similarity to the polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:13, is not sufficient reason to demonstrate that it is easy to obtain the claimed polynucleotide.

If it is probably possible to obtain the polynucleotide encoding a human WW1 factor (e.g. A consensus sequence which has high similarity among already known factor WW1 proteins, or documents which disclose consensus sequence, can be found.), we consider this invention may not be regarded as involving an inventive step.

Case 8

Utility (Industrial applicability): No

As utility of the claimed polynucleotide is not described in the specification or cannot be inferred, the claimed invention is not commercially applicable.

Enablement requirement: No

In Case8, there is a description that "An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:15" encodes a human DNA ligase. However, the reasons given by the applicant why the protein set forth in SEQ ID NO:14 is a factor WW1 protein are that the claimed polynucleiotide showed 30% homology to a polynucleotide encoding a known DNA ligase and 95% homology to the consensus sequence set forth in known DNA ligases which are based only on the similarity search.

In general, when the two polynucleotides (polypeptides) show a low similarity to each other, it is probable that two polynucleotides (polypeptides) do not have any specific functions in common. And it cannot be said necessarily that it is probable that the polynucleotide (polypeptide) has a specific function only under the condition that a polynucleotide (polypeptide) shows a high similarity to the consensus sequence. Therefore, we do not consider directly that the protein which is encoded by the claimed polynucleotide has DNA ligase activity based on 30% homology to a polynucleotide encoding a known DNA ligase and 95% homology to the consensus sequence set forth in known DNA ligases.

Moreover, as the specific function of the claimed polynucleotide also cannot be assumed with the common general knowledge as of the filing, the specific function of the claimed polynucleotide is not clear and it is not clear how to use the claimed polynucleotide.

Therefore, we consider there is no disclosure concerning the use of this polynucleotide in an industrial applicable way, thus the description of the invention is deemed insufficient for enabling a person skilled in the art to carry out the invention.

Inventive Step: No

Preparing a human DNA encoding protein is a well-known activity.

It is also the common general knowledge as of the filing to isolate human DNA encoding a certain protein which includes a consensus sequence by using a partial polynucleotide of a consensus sequence as a PCR primer for obtaining a polynucleotide encoding WW1, since polynucleotide encoding proteins with the same biological activities are in general highly homologous consensus sequences between mammalian species.

It is therefore obvious that the DNA encoding human DNA ligase can be isolated from the human cDNA library using the partial polynucleotide of a consensus sequence as a primer.

As advantageous effect cannot be acknowledged from the common general knowledge as of the filing, hence this invention cannot be regarded as involving an inventive step.

Case 9

Utility (Industrial applicability): Yes

Enablement requirement: Yes

In Case9, there is a description that "An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:17" encodes a human factor XX1. The given reason by the applicant that the claimed polynucleiotide showed 90% homology to a polynucleotide encoding a rat factor XX1 and that the protein which is encoded by the claimed poluynucleotide showed 95% homology to a rat factor XX1 is based only on similarity search.

In general, when two polynucleotides (polypeptides) show a high similarity to each other, it is probable that two polynucleotides (polypeptides) have any specific functions in common. Therefore, we consider that the protein encoded by the claimed polynucleotide has XX1 activity.

We consider the description of the invention to be sufficient for enabling a person skilled in the art to carry out the invention without certified experiment results.

Inventive Step: No

Preparing a human DNA encoding a protein is a well-known topic.
It is also common general knowledge to isolate a human DNA encoding a certain protein by using a partial nucleotide sequence of a non-human mammal encoding the same protein as a PCR primer for obtaining a polynucleotide encoding XX1, since polynucleotide encoding proteins with the same biological activities are in general highly homologous between mammalian species.
It is therefore obvious that the DNA encoding human factor XX1 can be isolated from the human cDNA library using the partial polynucleotide encoding rat factor XX1 written in document A as a primer.
As advantageous effect cannot be acknowledged from document A or the common general knowledge as of the filing, hence this invention cannot be regarded as involving an inventive step.

Case 10

Utility (Industrial applicability): Yes

Enablement requirement: Yes

In Case10, there is a description that "An isolated and purified polynucleotide consisting of the nucleotide sequence set forth in SEQ ID NO:19" encodes a human DNA ligase. The reason given by the applicant that the claimed polynucleiotide showed 80% homology to a polynucleotide encoding a known DNA ligase and 95% homology to the consensus sequence set forth in known DNA ligases are based only on similarity search.

In general, when two polynucleotides (polypeptides) show a high similarity to each other and a high similarity to the consensus sequence, it is probable that two polynucleotides (polypeptides) have any specific functions in common.

Therefore, we consider it probable that the protein encoded by the claimed polynucleotide has the DNA ligase activity.

We consider the description of the invention is deemed sufficient for enabling a person skilled in the art to carry out the invention without certified experiment results.

Inventive Step: No

Preparing a human DNA encoding a protein is a well-known activity.

It is also common knowledge to isolate a human DNA encoding a certain protein by using a partial nucleotide sequence of a non-human mammal encoding the same protein as a PCR primer for obtaining a polynucleotide encoding DNA ligase, since polynucleotide encoding proteins with the same biological activities are in general highly homologous between mammal species.

Therefore, it is obvious that the DNA encoding human DNA ligase can be isolated from the human cDNA library using the partial polynucleotide encoding a DNA ligase as a primer.

As advantageous effect cannot be acknowledged from the common general knowledge as of the filing, this invention cannot be regarded as involving an inventive step.